

CLAIMS

1. Use of at least one probe, with said probe being (i) capable of hybridizing to a genotype specific target region, present in an analyte strand, in the domain extending from the nucleotides at positions -291 to -66 of the 5' untranslated region of one of the HCV isolates, or with said probe being (ii) complementary to any of the above-defined probes, for genotyping HCV isolates present in a biological sample.

2. Process for genotyping HCV isolates present in a biological sample; comprising the steps of:

- contacting said sample in which the ribonucleotides or deoxyribonucleotides have been made accessible, if need be, under suitable denaturation, with at least one probe, with said probe being (i) capable of hybridizing to a region in the domain extending from nucleotides at positions -291 to -66 of the 5' untranslated region of one of the HCV isolates, or with said probe being (ii) complementary to any of the above-defined probes, and,

- detecting the complexes possibly formed between said probe and the nucleotide sequence of the HCV isolate to be identified.

3. Process according to claim 2, wherein a set of probes comprising at least two probes, is used.

4. Process according to anyone of claims 2 or 3, wherein the probe used targets a region of at least 5 nucleotides in one of the following domains:

a) the one extending from nucleotide at position -293 to nucleotide at position -278 (in Figures 2 and 4),

b) the one extending from nucleotide at position -275 to nucleotide at position -260 (in Figures 2 and 4),

c) the one extending from nucleotide at position -253 to nucleotide at position -238 (in Figures 2 and 4),

d) the one extending from nucleotide at position -244 to nucleotide at position -229 (in Figures 2 and 4),

e) the one extending from nucleotide at position -238 to nucleotide at position -223 (in Figures 2 and 4),

f) the one extending from nucleotide at position -170 to nucleotide at position -155 (in Figures 2 and 4),

- g) the one extending from nucleotide at position -141 to nucleotide at position -117 (in Figures 2 and 4),
- h) the one extending from nucleotide at position -83 to nucleotide at position -68 (in Figures 2 and 4),
- i) the one extending from nucleotide at position -103 to nucleotide at position -88 (in Figures 2 and 4),
- j) the one extending from nucleotide at position -146 to nucleotide at position -130.

5. Process according to claim 4, wherein for each type or subtype of HCV to be determined, a set of two different probes or a mixture of two different probes is used, each probe of the set or of the mixture targeting respectively different regions respectively chosen from among the following list of pairs of domains as defined in claim 4:

- * the one extending from nucleotide at position -170 to nucleotide at position -155 (in Figures 2 and 4) and the one extending from nucleotide at position -141 to nucleotide at position -117 (in Figures 2 and 4),
- * the one extending from nucleotide at position -170 to nucleotide at position -155 (in Figures 2 and 4) and the one extending from nucleotide at position -103 to nucleotide at position -88 (in Figures 2 and 4),
- * the one extending from nucleotide at position -141 to nucleotide at position -117 (in Figures 2 and 4) and the one extending from nucleotide at position -103 to nucleotide at position -88 (in Figures 2 and 4),
- * the one extending from nucleotide at position -170 to nucleotide at position -155 (in Figures 2 and 4) and the one extending from nucleotide at position -83 to nucleotide at position -68 (in Figures 2 and 4),
- * the one extending from nucleotide at position -141 to nucleotide at position -117 (in Figures 2 and 4) and the one extending from nucleotide at position -83 to nucleotide at position -68 (in Figures 2 and 4),
- * the one extending from nucleotide at position -170 to nucleotide at position -155 (in Figures 2 and 4) and the one extending from nucleotide at position -146 to nucleotide at position -130 (in Figures 2 and 4),
- * the one extending from nucleotide at position -132 to nucleotide at position -117 (in Figures 2 and 4) and the one extending from nucleotide at position -146 to nucleotide at position -130 (in Figures 2 and 4),
- * the one extending from nucleotide at position -146 to nucleotide at position -130 (in Figures 2 and 4) and the one extending from nucleotide at position -103 to nucleotide at position -88 (in Figures 2 and 4).

6. Probe having a sequence such that it targets at least one of the following sequences:

AAT TGC CAG GAC GAC C (SEQ ID NO 5)
TCT CCA GGC ATT GAG C (SEQ ID NO 6)
CCG CGA GAC TGC TAG C (SEQ ID NO 7)
TAG CGT TGG GTT GCG A (SEQ ID NO 8)
TTR CCG GRA AGA CTG G (SEQ ID NO 9)
TGR CCG GGC ATA GAG T (SEQ ID NO 10)
TTA CCG GGA AGA CTG G (SEQ ID NO 11)
TGA CCG GAC ATA GAG T (SEQ ID NO 12)
AAT CGC TGG GGT GAC C (SEQ ID NO 13)
TTT CTG GGT ATT GAG C (SEQ ID NO 14)
TCT TGG AGC AAC CCG C (SEQ ID NO 15)
TCT TGG AAC AAC CCG C (SEQ ID NO 16)
AAT YGC CGG GAT GAC C (SEQ ID NO 17)
TTC TTG GAA CTA ACC C (SEQ ID NO 18)
TTT CCG GGC ATT GAG C (SEQ ID NO 19)
TTG GGC GYG CCC CCG C (SEQ ID NO 20)
CCG CGA GAT CAC TAG C (SEQ ID NO 21)
CCG GGA AGA CTG GGT C (SEQ ID NO 22)
CCG GAA AGA CTG GGT C (SEQ ID NO 23)
ACC CAC TCT ATG CCC G (SEQ ID NO 24)
ACC CAC TCT ATG TCC G (SEQ ID NO 25)
ATA GAG TGG GTT TAT C (SEQ ID NO 26)
TCT GCG GAA CCG GTG A (SEQ ID NO 27)
AAT TGC CAG GAY GAC C (SEQ ID NO 28)
GCT CAG TGC CTG GAG A (SEQ ID NO 29)
CCG CGA GAC YGC TAG C (SEQ ID NO 30)
CCC CGC AAG ACT GCT A (SEQ ID NO 31)
CGT ACA GCC TCC AGG C (SEQ ID NO 32)
GGA CCC AGT CTT CCT G (SEQ ID NO 33)
TGC CTG GTC ATT TGG G (SEQ ID NO 34)
TKT CTG GGT ATT GAG C (SEQ ID NO 35)
CCG CAA GAT CAC TAG C (SEQ ID NO 36)
GAG TGT TGT ACA GCC T (SEQ ID NO 37)
AAT CGC CGG GAT GAC C (SEQ ID NO 38)
GAG TGT TGT GCA GCC T (SEQ ID NO 39)
AAT CGC CGG GAC GAC C (SEQ ID NO 40)
AAT GCC CGG CAA TTT G (SEQ ID NO 41)

AAT CGC CGA GAT GAC C (SEQ ID NO 42)
AAT GCT CGG AAA TTT G (SEQ ID NO 43)
GAG TGT CGA ACA GCC T (SEQ ID NO 44)
AAT TGC CGG GAT GAC C (SEQ ID NO 45)
TCT CCG GGC ATT GAG C (SEQ ID NO 46)
AAT TGC CGG GAC GAC C (SEQ ID NO 47)
GGG TCC TTT CCA TTG G (SEQ ID NO 48)
AAT CGC CAG GAT GAC C (SEQ ID NO 49)
TGC CTG GAA ATT TGG G (SEQ ID NO 50)
GAG TGT CGT ACA GCC T (SEQ ID NO 51)
AGT YCA CCG GAA TCG C (SEQ ID NO 52)
GGA ATC GCC AGG ACG A (SEQ ID NO 53)
GAA TCG CCG GGT TGA C (SEQ ID NO 54)
GAG TGT TGT ACA GCC TCC (SEQ ID NO 93)
TGC CCG GAA ATT TGG GC (SEQ ID NO 94)
TGC CCG GAG ATT TGG G (SEQ ID NO 95)
GAG TGT CGA ACA GCC TC (SEQ ID NO 96)

wherein Y represents T or C

K represents G or T

and R represents G or A

- or the corresponding sequence wherein T has been replaced by U,
- or the sequences which are complementary to the above-defined sequences.

7. Set of two probes or mixtures of two probes wherein each of the two probes respectively targets different regions chosen from among the following list of pairs of domains as defined in claim 4:

* the one extending from nucleotide at position -170 to nucleotide at position -155 (in Figures 2 and 4) and the one extending from nucleotide at position -141 to nucleotide at position -117 (in Figures 2 and 4),

* the one extending from nucleotide at position -170 to nucleotide at position -155 (in Figures 2 and 4) and the one extending from nucleotide at position -103 to nucleotide at position -88 (in Figures 2 and 4),

* the one extending from nucleotide at position -141 to nucleotide at position -117 (in Figures 2 and 4) and the one extending from nucleotide at position -103 to nucleotide at position -88 (in Figures 2 and 4),

* the one extending from nucleotide at position -170 to nucleotide at position -155 (in Figures 2 and 4) and the one extending from nucleotide at position -83 to nucleotide at position -68 (in Figures 2 and 4).

* the one extending from nucleotide at position -141 to nucleotide at position -117 (in Figures 2 and 4) and the one extending from nucleotide at position -83 to nucleotide at position -68 (in Figures 2 and 4),

* the one extending from nucleotide at position -170 to nucleotide at position -155 (in Figures 2 and 4) and the one extending from nucleotide at position -146 to nucleotide at position -130 (in Figures 2 and 4),

* the one extending from nucleotide at position -132 to nucleotide at position -117 (in Figures 2 and 4) and the one extending from nucleotide at position -146 to nucleotide at position -130 (in Figures 2 and 4),

* the one extending from nucleotide at position -146 to nucleotide at position -130 (in Figures 2 and 4) and the one extending from nucleotide at position -103 to nucleotide at position -88 (in Figures 2 and 4).

8. Process according to any one of claims 2 to 7, for genotyping HCV isolates belonging to at least one of the following HCV types: HCV type 1, HCV type 2, HCV type 3, HCV type 4, HCV type 5, HCV type 6, from a biological sample liable to contain it, comprising the steps of

- contacting said sample in which the ribonucleotides or deoxyribonucleotides have been made accessible, if need be, under suitable denaturation, with at least one probe being (i) capable of hybridizing to a region being in the domain extending from nucleotide at position -291 to nucleotide at position -66 of the 5' untranslated region of HCV isolates or with said probe being (ii) complementary to the above-defined probes, and;

- detecting the complexes possibly formed between said probe and the target region, and,

- inferring the HCV types present from the observed hybridization patterns

9. Process according to claim 8, for genotyping HCV isolates as belonging to at least one of the following HCV types: HCV type 1, HCV type 2, HCV type 3 or HCV type 4, HCV type 5, HCV type 6, wherein the probes used are able to target at least one of the following target regions, or said regions wherein T has been replaced by U, or the regions which are complementary to the above-said regions:

for HCV type 1 and 6: AAT TGC CAG GAC GAC C (No. 5)
TCT CCA GGC ATT GAG C (No. 6)

AAT TGC CAG GAY GAC C (No. 28)

GCT CAG TGC CTG GAG A (No. 29)

TAG CGT TGG GTT GCG A (No. 8)

TTR CCG GRA AGA CTG G (No. 9)

TGR CCG GGC ATA GAG T (No. 10)

TTA CCG GGA AGA CTG G (No. 11)

for HCV type 1:

for HCV type 2:

TGA CCG GAC ATA GAG T (No. 12)
 CGT ACA GCC TCC AGG C (No. 32)
 CCG GCA AGA CTG GGT C (No. 22)
 CCG GAA AGA CTG GGT C (No. 23)
 ACC CAC TCT ATG CCC G (No. 24)
 ACC CAC TCT ATG TCC G (No. 25)
 ATA GAG TGG GTT TAT C (No. 26)
 GGA CCC AGT CTT CCT G (No. 33)
 TGC CTG GTC ATT TGG G (No. 34)

for HCV type 3: AAT CGC TGG GGT GAC C (No. 13)
 TTT CTC GGT ATT GAG C (No. 14)
 CCG CGA GAT CAC TAG C (No. 21)
 CCG CAA GAT CAC TAG C (No. 36)
 GAA TCG CCG GGT TGA C (No. 54)
 for HCV type 4 and 5: AAT YGC CGG GAT GAC C (No. 17)

for HCV type 4: TTC TTG GAA CTA ACC C (No. 18)
 for HCV type 4, 3c and 3b: TTT CCG GGC ATT GAG C (No. 19)
 for HCV type 4 and 3b: AAT CGC CGG GAT GAC C (No. 38)

for HCV type 4:
 GAG TGT TGT ACA GCC T (No. 37)
 GAG TGT TGT GCA GCC T (No. 39)
 AAT CCC CGG GAC GAC C (No. 40)
 AAT CCC CGG CAA TTT G (No. 41)
 AAT CGC CGA GAT GAC C (No. 42)
 AAT GCT CGG AAA TTT G (No. 43)
 AAT CGC CAG GAT GAC C (No. 49)
 TGC CTG GAA ATT TGG G (No. 50)
 GGA ATC GCC AGG ACG A (No. 53)

for HCV type 5:
 AAT TGC CGG GAT GAC C (No. 45)
 AAT TGC CGG GAC GAC C (No. 47)
 TCT CCG GGC ATT GAG C (No. 46)
 GAG TGT CGA ACA GCC T (No. 44)

for HCV type 6:
 GGG TCC TTT CCA TTG G (No. 48)

wherein Y represents C or T, and K represents G or T,
 or the probes used are a set of two probes chosen from among the above-defined probes.

10. Process according to claim 9, also comprising the discrimination and classification of subtypes of HCV, wherein besides at least one probe capable of hybridising with a certain type of HCV as defined in claim 9, at least one of the probes targeting the following target regions is used, or said regions wherein T is

replaced by U, or said regions which are complementary to the above defined regions,

for HCV type 1, subtype 1a:

CCC CGC AAG ACT GCT A (No. 31)

for HCV type 1, subtype 1b:

CCG CGA GAC TGC TAG C (No. 7)

CCG CGA GAC YGC TAG C (No. 30)

wherein Y represents C or T,

for HCV type 2, subtype 2a:

TTR CCG GRA AGA CTG G (No. 9)

TGR CCG GGC ATA GAG T (No. 10)

CCG GGA AGA CTG GGT C (No. 22)

ACC CAC TCT ATG CCC G (No. 24)

wherein R represents A or G,

for HCV type 2, subtype 2b:

TTA CCG GGA AGA CTG G (No. 11)

TGA CGG GAC ATA GAG T (No. 12)

CCG GAA AGA CTG GGT C (No. 23)

ACC CAC TCT ATG TCC G (No. 25)

for HCV type 2, subtype 2c:

GGA CCC AGT CTT CCT G (No. 33)

TGC CTG GTC ATT TGG G (No. 34)

for HCV type 3, subtype 3a:

AAT CGC TGG GGT GAC C (No. 13)

TTT CTG GGT ATT GAG C (No. 14)

TKT CTG GGT ATT GAG C (No. 35)

wherein K represents G or T,

for HCV type 3, subtype 3b:

TTT CCG GGC ATT GAG C (No. 19)

AAT CGC CGG GAT GAC C (No. 38)

CCG CGA GAT CAC TAG C (No. 21)

for HCV type 3, subtype 3c:

GAG TGT CGT ACA GCC T (No. 51)

GAA TCG CCG GGT TGA C (No. 54)

TTT CCG GGC ATT GAG C (No. 19)

CCG CGA GAC TGC TAG C (No. 7)

for HCV type 4, subtype 4a or 4d:

AAT CGC CGG GAT GAC C (No. 38)

TTT CCG GGC ATT GAG C (No. 19)

for type 4, subtype 4b :

AAT CGC CGG GAT GAC C (No. 38)

AAT GCC CGG CAA TTT G (No. 41)

AAT CGC CGG GAC GAC C (No. 40)

for type 4, subtype 4c:

AAT CGC CGA GAT GAC C (No. 42)
AAT GCT CGG AAA TTT G (No. 43)
TGC CTG GAA ATT TGG G (No. 50)
GGA ATC GCC AGG ACG A (No. 53)
CCG CGA GAC TGC TAG C (No. 7)

for type 4, subtype 4e:

AAT CGC CGG GAC GAC C (No. 40)
GAG TGT TGT GCA GCC T (No. 39)
AAT GCC CGG CAA TTT G (No. 41)

for type 4, subtype 4f:

TTT CCG GGC ATT GAG C (No. 19)
AAT CGC CGG GAT GAC C (No. 38)
GAG TGT CGT ACA GCC T (No. 51)
CCG CGA GAC TGC TAG C (No. 7)

for type 4, subtype 4g (provisional):

TGC CTG GAA ATT TGG G (No. 50)
GGA ATC GCC AGG ACG A (No. 53)

for type 4, subtype 4h (provisional):

AAT CGC CAG GAT GAC C (No. 49)
TGC CTG GAA ATT TGG G (No. 50)

or the probes used are a set of two probes chosen from among the defined probes,

and when there are only two subtypes of a type, these above-mentioned probes being liable to determine, by exclusion, the subtype deduced from the fact that they do not target one of the above-mentioned regions.

11. Process according to anyone of claims 2 to 10, wherein the HCV types or subtypes to be differentiated are identified by means of universal probes for HCV, such as the ones targeting one of the following regions:

TTG GGC GYG CCC CCG C (No. 20)
TCT GCG GAA CCG GTG A (No. 27)

12. Process according to anyone of claims 2 to 11 wherein the hybridisation step is preceded by an amplification step of the deoxyribonucleotide orribonucleotide containing the region to target, advantageously comprising the following steps:

- contacting the biological sample liable to contain the isolate to be typed or subtyped with a set of primers, flanking the region to target, with said primers being complementary to conserved regions of the HCV genome, and preferably primers being complementary to the 5' untranslated conserved

regions of the HCV genome, with said primers preferably having at least 15 contiguous nucleotides, with said contiguous nucleotides being respectively complementary to sequences chosen from the region extending from nucleotide -341 to nucleotide -171 and from the region extending from nucleotide -67 to nucleotide -1 (of figures 2 and 4),

- amplifying the target region, for instance via a polymerase chain reaction by means of the above-mentioned set of primers and possibly incorporating a label, such as digoxigenin or biotin into the amplified target sequence, with said amplifying being repeated between 20 and 80 times, advantageously between 30 and 50 times.

13. Process according to claim 12, wherein the amplification consists of a double PCR step, each step involving a specific set of primers, with (the) said first step involving outer primers selected from the region extending from nucleotide -341 to nucleotide -186 and from the region extending from nucleotide -52 to nucleotide -1, and more particularly the following set:

CCC TGT GAG GAA CTW CTG TCT TCA CGC (No. 1)

GGT GCA CGG TCT ACG AGA CCT (No. 2)

or their complements,

wherein W represents A or T, and with the second step involving nested primers selected from the region extending from nucleotide -326 to nucleotide -171 and from the region extending from nucleotide -68 to nucleotide -1 and, more particularly the following set:

TCT AGC CAT GGC GTT AGT RYG AGT GT (No. 3)

CAC TCG CAA GCA CCC TAT CAG GCA GT (No. 4)

wherein R represents A or G and Y represents T or C,

or their complements.

14. Process for the simultaneous genotyping of all HCV isolates contained in a biological sample according to anyone of claims to 2 to 13, comprising the step of contacting one of the following elements:

- either said biological sample in which the genetic material is made available for hybridization,
- or the purified genetic material contained in said biological sample,
- or single copies derived from the purified genetic material,

- or amplified copies derived from the purified genetic material,
with a solid support on which probes according to anyone of claims 2 to 13 have
been previously immobilized.

15. Process according to any one of claims 2 to 14, comprising the steps of contacting anyone of the probes according to anyone of claims 2 to 14, with one of the following elements:

- either a biological sample in which the genetic material is made available for hybridization,
 - or the purified genetic material contained in said biological sample,
 - or a single copy derived from the purified genetic material,
 - or an amplified copy derived from the purified genetic material,
- with said elements being previously immobilized on a support.

16. Process for detecting and identifying novel HCV types or subtypes, different from the known types or subtypes, comprising the steps of:

- determining to which known types or subtypes, the HCV isolates present in the biological sample belong to, according to the process as defined in claim 2, possibly with said biological sample being previously determined as containing HCV, possibly by means of HCV antigen or antibody assays or with a universal probe for HCV, such as those defined in claim 11,
- in the case of observing a sample which does not hybridize positively with at least one of the probes able to target the regions chosen from any of the domains as defined in claim 4, sequencing the complete genome of the HCV type present in the sample, or, alternatively sequencing that (the) portion(s) of the 5' untranslated region of the sample corresponding to a new type and/or subtype to be determined.

17. Process for the detection and identification of novel HCV types and/or subtypes, present in a biological sample, which are different from type 1, type 2, type 3, type 4, type 5 and type 6, in the case of identifying a novel type; and which are different from subtypes 1a and 1b for a type 1 HCV isolate, from subtypes 2a and 2b for a type 2 isolate, from subtypes 3a 3b, and 3c for a type 3 isolate, from subtypes 4a, 4b, 4c 4d, 4e, 4f, 4g(provisional) and 4h(provisional) for

a type 4 isolate, in the case of identifying a novel subtype, and comprising the steps of:

- determining to which known type(s) or subtype(s) the

HCV isolate(s) present in the biological sample to be analyzed belongs, according to the process according to anyone of claims 2 to 14, possibly with said biological sample being previously determined as containing HCV, possibly by means of HCV antigen or antibody assays or with a universal probe for HCV such as the one defined in claim 11,

- in the case of observing a sample which does not hybridize to at least one of the probes able to target the regions chosen from any of the type specific or subtype specific domains as defined in claims 9 and 10, more particularly not hybridizing with SEQ ID NO 5, 28 and 6 for type 1, with SEQ ID NO 8 to 12 or 22 to 26 and 32 to 34 for type 2, with SEQ ID NO 13, 14, 36, 21 or 54 for type 3, and with SEQ ID NO 17, 18, 19, 37 to 43, 49, 50 and 53 for type 4; and with SEQ ID NO 7 and 30 for subtype 1b, with SEQ ID NO 31 for subtype 1a, with SEQ ID NO 9, 10, 22 or 24 for subtype 2a, with SEQ ID NO 11, 12, 23 or 25 for subtype 2b, with SEQ ID NO 33 or 34 for subtype 2c, with SEQ ID NO 13, 14 or 35 for subtype 3a, with SEQ ID NO 38, 21 and 19 for subtype 3b, 4a or 4d, with SEQ ID NO 38 or 41 for subtype 4b; with SEQ ID NO 42 or 43 for subtype 4c; with SEQ ID NO 39, 40, or 41 for subtype 4e, with SEQ ID NO 51, 38, 19 or 7; with SEQ ID NO 49 or 50 for the putative subtype 4h; with SEQ ID NO 50 or 53 for the putative subtype 4g, sequencing the complete genome of the HCV type present in the sample, or, alternatively sequencing that (the) portion(s) of the 5' untranslated region of the sample corresponding to a new type and/or subtype to be determined.

18. A method for determining the type(s) as well as the subtypes(s) of HCV, and/or HIV, and/or HBV and/or HTLV present in a biological sample, which comprises the steps of:

- providing

* at least one of the probes as defined in any of claims 1 to 8, preferably the probes as defined in claims 9 and 10, enabling the genotyping (typing and/or subtyping) of HCV, and at least one of the following probes:

* probes capable of detecting oligonucleotides of HIV types 1 and/or 2 which can be present in said biological sample, and/or

* probes capable of detecting oligonucleotides of HBV subtypes and/or surface antigen (sAg) mutants and/or core antigen (cAg) mutants which can be present in said biological sample, and/or

* probes capable of detecting oligonucleotides of HTLV-I and/or HTLV-II suspected to be in the biological sample,

- possibly providing a set of primers as defined in claims 12 or 13, as well at least one of the following primers: sets of primers to respectively amplify HIV, and/or HBV and/or HTLV oligonucleotides, by means of PCR reaction and amplifying the oligonucleotides of HCV, and either HBV and/or HIV and/ or HTLV possibly present in the biological sample,

- contacting

* the biological sample in which the genetic material is made available for hybridization,

* or the purified genetic material contained in said biological sample,

* or single copies derived from the purified genetic material,

* or amplified copies derived from the purified genetic material,

with the probes defined above under conditions which allow hybridization between the probes and the target sequences of isolates of HCV and at least one of the following viruses: HBV and/or HIV and/or HTLV,

- detecting the complexes possibly formed between the probes used and the target regions possibly present in the biological sample.

19. Solid support, particularly a membrane strip containing, on known locations of its surface, the following probes, or their complements, or the above-said probes wherein T has been replaced by U:

- SEQ ID NO 5, NO 6, NO 7, NO 8, NO 9, NO 10, NO 11, NO 12, NO 13, NO 14, NO 15, NO 16, NO 17, NO 18, NO 19, NO 20, NO 21, NO 22, NO 23, NO 24, NO 25, NO 26, NO 27, NO 28 to NO 54 and SEQ ID NO 93 to 96, according to claims 9 and 10, as well as a control to determine if there is hybridization between these probe and the ribo or deoxyribonucleotide strands of HCV, liable to be contained in a biological sample in which HCV isolates are to be discriminated.

20. Kit for the *in vitro* discrimination of any isolate of HCV, with said kit containing

- means to identify the presence of HCV isolate,

- at least one probe as defined in claim 1,

- a buffer or components necessary for producing the buffer enabling hybridization reaction between these probes and the DNAs and/or RNAs of HCV isolates to be carried out;

- when appropriate, means for detecting the hybrids resulting from the preceding hybridization.

21. Kit for typing at least one HCV isolate, from a biological sample liable to contain it, and for classifying it according to the HCV type and subtype, with said kit containing

- possibly one probe as defined in claim 11,

- at least one probe selected among any of those according

to claims 2 to 10,

- a buffer or components necessary for producing the buffer enabling hybridization reaction between these probes and the DNAs and/or RNAs of HCV isolates to be carried out;

- when appropriate, means for detecting the hybrids resulting from the preceding hybridization.

22. Kit for typing HCV isolates belonging to at least one of the following HCV isolates: HCV type 1, HCV type 2, HCV type 3, HCV type 4, HCV type 5, HCV type 6 with said kit containing at least one of the probes according to claim 9,

- the buffer or components necessary for producing the buffer enabling hybridization reaction between these probes and the cDNAs and/or RNAs of the above-mentioned HCV isolates to be carried out;

- when appropriate, means for detecting the hybrids resulting from the preceding hybridization.

23. Kit for the discrimination and classification of HCV types and subtypes, with said kit containing:

- at least one of the probes according to claims 9 or 10,

- the buffer or components necessary for producing the buffer enabling hybridization reaction between these probes and the DNAs and/or RNAs of the above-mentioned HCV isolates to be carried out;

- when appropriate, means for detecting the hybrids resulting from the preceding hybridization.

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x 2*